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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,902	04/26/2004	Hong Zhou	HACK 206	8225

24972 7590 09/14/2007
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EXAMINER	
DEBERRY, REGINA M	

ART UNIT	PAPER NUMBER
1647	

MAIL DATE	DELIVERY MODE
09/14/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/031,902	ZHOU ET AL.	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40-70* is/are pending in the application.

4a) Of the above claim(s) *47,50,52,53,55,57,58,61 and 70* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-46,48,49,51,54,56,59,60 and 62-69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Status of Application, Amendments and/or Claims

Claims 1-39 were canceled (18 January 2002). Claims 47, 50, 52, 53, 55, 57 and 58 were withdrawn from further consideration (17 October 2006). New claims 59-70 were submitted (20 February 2007). The amendment filed 20 February 2007 has been entered.

Newly submitted claims 59, 61 and 70 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Applicant elected Group I, claims 40-54, 56, drawn in part to an isolated nucleic acid molecule, isolated polypeptide, and a method of treating a condition characterized by abnormal bone resorption comprising administering a polypeptide. Applicant also elected species SEQ ID NO:36 (isolated nucleic acid), which includes the isolated polypeptide encoded by the nucleic acid. Please see the previous Office Action (17 October 2006).

Claim 59 (SEQ ID NOs:41 and 42) and claim 61 (SEQ ID NO:20) are drawn to isolated polypeptides comprising new and non-elected SEQ ID Nos. Claim 70 is drawn to a method of treating a condition characterized by abnormal bone resorption comprising administering an isolated nucleic acid.

Since Applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Only SEQ ID NO:40 from claim 59 will be examined, as it is drawn to the polypeptide encoded by elected SEQ ID NO:36. Claims 61 and 70 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR

1.142(b) and MPEP § 821.03. Claims 47, 50, 52, 53, 55, 57, 58, 61 and 70 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Group (or SEQ ID NO:), there being no allowable generic or linking claim.

Claims 40-46, 48, 49, 51, 54, 56, 59, 60, 62-69 are under examination. The instant claims are examined to the degree that they reflect the elected invention and no other embodiments.

Withdrawn Objections And/Or Rejections

The rejection to claims 40-46, 48, 49, 51, 54 and 56 under 35 U.S.C. 112, second paragraph, as set forth at pages 2-3 of the previous Office Action (17 October 2006), is *withdrawn* in view of the amendment (20 February 2007).

Sequence Rules

The specification is not in compliance with 37 CFR 1.821-1.825 of the Sequence Rules and Regulations. The basis for this rejection is set forth at page 3 of the previous Office Action (17 October 2006).

In the response dated 05 June 2007, Applicant states, "responsive to the action dated May 24, 2007, Applicants will attempt to address the Examiner's issue". Applicant argues that SEQ ID NOS: are not provided in replacement page 18 because all of these sequence were identified previously. Applicant directs the Examiner's attention to page 17. Applicant argues that a SEQ ID NO: need only be provided the

first time it is presented in a specification, not each time. Applicant argues that replacement page 18 is provided.

Applicant's arguments have been fully considered but are not found persuasive. Applicant argues that a SEQ ID NO: need only be provided the first time it is presented in a specification, not each time, but does not provide basis for this assertion. MPEP 2421.02 states the following: Basically, the sequence rules define a set of symbols and procedures that are both mandatory and the only way that an applicant is permitted to describe information about a sequence that falls within the definitions used in the rules. Thus, 37 CFR 1.821 defines a "sequence" and a "Sequence Listing" for the purpose of the rules, the requirements for specific symbols, and formats for the "Sequence Listing," the requirement for a computer readable form (CRF) of the "Sequence Listing," and the deadlines for complying with the requirements. 37 CFR 1.822 to 37 CFR 1.824 set forth detailed descriptions of the requirements that are mandatory for the presentation of sequence data, and 37 CFR 1.825 sets forth procedures that are available to an applicant in the event that amendments to the sequence information or replacement of the computer readable copy become necessary. The sequence rules embrace all unbranched nucleotide sequences with ten or more bases and all unbranched, non-D amino acid sequences with four or more amino acids, provided that there are at least 4 "specifically defined" nucleotides or amino acids. **The rules apply to all sequences in a given application, whether claimed or not. All such sequences are relevant for the purposes of building a comprehensive database and properly assessing prior art. It is therefore essential that all sequences, whether only disclosed or also**

claimed, be included in the database. MPEP 2422(d) states the following: Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing " in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO: " in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application.

Applicant only needs to add the proper SEQ ID NO: the sequences. This does not require adding more sequences to the Sequence Listing. The Examiner stated in the previous Office Action that the specification refers to sequences in Figures 8A-8C; Figure 9; Figure 18B and on pages 13, lines 12 and 20; page 14, lines 15-16; page 15, lines 1-2 and 16-17; page 19, lines 1-4; page 30, lines 26-27 and 33; page 31, lines 1-6 and page 40, lines 14, 16 and 21, but does not identify the sequences by their sequence identifiers. Sequences appearing in drawings should be referenced in the corresponding Brief Description thereof. See 37 C.F.R. §1.58(a) and §1.83. The Examiner is unclear how replacement page 18 corrects the instant sequence problem, as this page was not cited. Adding the proper sequence identifier to the sequences recited above would be remedial.

The entire specification should be examined for proper sequence identifiers. Appropriate correction is required. Applicant must submit a response to this Office Action and comply with the sequence rules within the statutory period set for response to this Office Action.

Claim Rejections - 35 USC § 112, First Paragraph, Written Description

Claims 40-46, 48, 49, 51, 54, 56 (and new claims 60, 62-69) remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The basis for this rejection is set forth at pages 8-10 of the previous Office Action (17 October 2006).

Applicant argues that regarding the written description rejection, the language "modulators of function or expression" has been deleted from the claims. Applicant argues that in order to envision the "detailed chemical structure of the encompassed polynucleotide or translated polypeptides", all one has to do is review the sequence listings, as was shown supra. Applicant states that the cases relied upon by the Examiner to support the position, is apposite, since in both cases, no molecules encompassed by the claims were disclosed. Applicant contends that such is clearly not the case here, and was shown supra.

Applicant's arguments have been fully considered but are not deemed persuasive. Claim 40 still recites, "..has greater than 80% sequence identity with one or more of the sequences set out in (i)". The courts have specifically stated that the skilled artisan cannot envision the *detailed chemical structure* of an encompassed polynucleotide/polypeptide until the structure is disclosed, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. In the instant case, SEQ ID NO:36 has been disclosed, but no native

sequence variants thereof have been disclosed regardless of whether or not they encode a protein, which inhibits osteoclast differentiation from haematopoietic cell precursors. There is substantial variability among the species of nucleic acids of SEQ ID NO:36 encompassed within the scope of claim 40 that is not described. The specification teaches only the structural feature of SEQ ID NO:36. The instant claim encompasses genes yet to be discovered. There is no disclosure regarding the coding capacity of any of the variants cited. Defining the variant in functional terms would not suffice in the absence of a disclosure of structural features or elements of a cDNA that would encode a protein. The specification does not place any limit on the number of nucleotides substitutions, deletions, insertions and/or additions that may be made to SEQ ID NO:36. The specification does not provide any guidance as to what changes should be made and which regions are functionally and structurally critical. There is no description of variants of SEQ ID NO:36 that exist, while still maintaining function of the protein. The disclosure fails to describe the common attributes or characteristics that identify the members of the genus, and because the genus is variant, SEQ ID NO:36 alone is insufficient to describe the genes. The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

NEW CLAIM REJECTIONS/OBJECTIONS

Claim Rejections-35 USC § 112, First Paragraph, Written Description (New Matter)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Newly amended claim 49 and new claims 62, 64, 67 and 68 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.**

The specification as originally filed does not provide support for the invention as now claimed: "the nucleic acid molecule according to claim 40, **which encodes a protein which inhibits differentiation** of haematopoietic stem cells in osteoclast progenitor cells" (claim 49); "the isolated polypeptide according to claim 54, whose expression is differentially regulated by PTH or PTHrP" (claim 62); "an isolated polypeptide selected from the group consisting of an extracellular domain, a transmembrane domain, and a cytoplasmic domain of the polypeptide according to claim 54" (claim 64); "a diagnostic kit for detection of abnormalities in the structure, expression or control of a type II membrane polypeptide expressed on the osteoblast cell surface, selected from the group consisting of osteoclast inhibitory lectin (OCIL) and OCIL-related protein, comprising a nucleic acid according to claim 40, or a fragment thereof capable of hybridizing to a nucleic acid according to claim 40" (claim 67); "a diagnostic kit for detection of abnormalities in the structure, expression or control of a type II membrane polypeptide expressed on the osteoblast cell

surface, selected from the group consisting of osteoclast inhibitory lectin (OCIL) and OCIL-related protein, comprising a polypeptide according to claim 54" (claim 68).

Applicant's amendment, filed 20 February 2007, states that the added claims encompass subject matter within the elected invention and that amendments to the claims are directed to the various rejections. Applicant, however, does not provide direction for the written description for the above-mentioned "limitations" and the Examiner cannot locate the wording or connotation of the instant claims.

The specification as filed does not provide a written description or set forth the metes and bounds of this "limitations". The instant claims now recite limitations that were not clearly disclosed in the specification as filed, and now change the scope of the instant disclosure as-filed.

Applicant is required to cancel the new matter in the response to this Office action. Alternatively, Applicant is invited to provide *specific written support* for the "limitations" indicated above or rely upon the limitations set forth in the specification as filed.

Claim Rejections - 35 USC § 112, First Paragraph, Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 40-46, 48, 49, 51, 54, 56, 59, 60, 62-69 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

An isolated nucleic acid molecule which comprises a sequence encoding a protein which inhibits osteoclast differentiation from haematopoietic cell precursors, selected from the group consisting of osteoclastinhibitory lectin (OCIL) and OCIL-related protein, and which (i) hybridizes to SEQ ID NO: 36 (elected species) at 65°C in a hybridization buffer containing 4 x SSPE, 5 x Denhardt's solution, 0.5% sodium dodecyl sulfate for 24 hr, followed by sequential washing in 2 x SSC at 65°C for 15 min, 2 x SSC with 0.1% SDS at 65°C for 30 min, and 0.1 x SSX at 65°C for 10 min,

does not reasonably provide enablement for:

(ii) has greater than 80% sequence identity with one or more of the sequences set out in (i).

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicant argues that the Examiner has not supplied any evidence to support the position that sequence similarity less than 100% raises a question as to biological activity. Applicant argues that it is well known, for example that murine, rat, feline, canine, ursine, etc., molecules comparable to a human molecule will vary in sequence, but will have similar properties. Applicant argues that is it black letter law that a claim does not have to be enabled for every molecule it covers. Applicant contends that experimentation is permissible to discover those which are enabled, as long as experimentation is not undue. Applicant maintains that the claims limit the scope of molecules embraced thereby with the hybridization language. Applicant argues that the

specification teaches how one of ordinary skill in the art could determine if a molecule which satisfies the structural characteristics of the claims, would also share the recited properties.

Applicant's arguments have been fully considered but are not deemed persuasive. Contrary to Applicant's assertion, the Examiner submitted Wells (Wells, Biochemistry 29:8509-8517, 2000) to show that the protein's active/binding site must assume the proper three-dimensional configuration to be active. Wells teaches that conformation is dependent upon surrounding residues and that substitution of non-essential residues can often destroy activity. Furthermore, the instant claims do not recite murine, rat, feline, canine molecules of SEQ ID NO:36. The instant claims recite, "..has greater than 80% sequence identity..". The enablement issue is judged against the well-established Wands factors, as recited in the previous Office Action. The issue here is the breadth of the claim. Claim 40 encompasses a genus of nucleic acid molecules of any sequence greater than 80% sequence with the sequences set out in (i). The instant disclosure would not be found to be enabling for the whole genus because the instant disclosure fails to show which portions of SEQ ID NO:36 are critical to the activity of the protein encoded by SEQ ID NO:36 and what modifications (e.g., substitutions, deletions or additions) one can make to SEQ ID NO:36 will result in protein mutants with the same functions as the wild-type protein encoded by SEQ ID NO:36. While there is no requirement for all species of a genus to have exactly same properties, the disclosure has to enable an artisan to make and use the genus. To satisfy the enablement requirement, the disclosure must teach how to make and use the

invention. In the instant case, the disclosure must teach an artisan how to make and use the whole genus, not just the full length nucleic acid sequence of SEQ ID NO:36, which encodes a protein which inhibits osteoclast differentiation form haematopoietic cell precursors, because the majority of the species of the genus do not obviously encode the instant protein.

Undue experimentation is a conclusion reached by weighing all of the Wands factors. If one skilled in the art can readily anticipate the effect, than there is predictability in the art. In this case, the art is unpredictable based on the evidence provided. The evidence for the degree of predictability in the art also relates to the amount of direction needed in the specification. The instant claims encompass sequence variants. Without sufficient guidance, the changes which can be made in the structure and still maintain sufficient activity is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. A considerable amount of time is permissible for the quantity of experimentation needed to make and/or use the invention based on the disclosure. However this depends on if the invention is routine or if the skilled artisan is given sufficient direction or guidance. In the instant case, the experimentation is not routine and the specification has provided no guidance.

Claim Objections

Claim 51 is objected to because "nucleic" is misspelled. Appropriate correction is required.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

RMD
9/6/07

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